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(54) Titre : UTILISATION D'ACIDES CYCLOHEXANE POLYCARBOXYLIQUES COMME PLASTIFIANTS POUR LA PRODUCTION DE MATIERES PLASTIQUES DONT LA VALORISATION EST FAVORABLE SUR LE PLAN TOXICOLOGIQUE

(54) Title: USE OF CYCLOHEXANE POLYCARBOXYLIC ACIDS AS PLASTICIZERS IN THE PRODUCTION OF PLASTICS WHICH ARE RATED TOXICOLOGICALLY FAVOURABLE

(57) Abrégé/Abstract:
The invention relates to the use of a cyclohexane polycarboxylic acid or of one of its derivatives, or of a mixture of one or more of said acids as plasticizers in the production of plastics which are rated toxicologically favourable. In animal experiments, using rodents, to which a daily oral dose of 1000 mg/kg body weight of the corresponding cyclohexane polycarboxylic acid, or a derivative thereof, or a mixture of two or more of said acids is administered by oesophageal tube over a period of at least 14 days, said dose, in comparison to untreated control animals, leads neither to a significant increase in the weight of the liver after treatment, nor to a doubling of the specific cyanide-insensitive palmitoyl-CoA oxidase activity, measured in the liver homogenisate.

USE OF CYCLOHEXANE POLYCARBOXYLIC ACIDS AS PLASTICIZERS IN THE PRODUCTION OF PLASTICS WHICH ARE RATED TOXICOLOGICALLY FAVOURABLE

The present invention relates to the use of toxicologically advantageous cyclohexanepolycarboxylic acids and derivatives thereof, e.g. esters and/or anhydrides, as plasticizers for preparing toxicologically advantageous plastics.

The plasticizers used in plastics, e.g. PVC, have hitherto very often been phthalic esters, e.g. dibutyl, dioctyl or diisononyl phthalate, as seen, for example, in FR-A 23 97 131. However, recently these have been said to give health concerns, and their use in plastics for producing children's toys, for example, is coming under increasingly severe criticism and is now prohibited in some countries. Tests on animals have now shown that phthalates can cause peroxisome proliferation, which has a causal connection with the liver tumors which occur in long-term studies on mice and rats.

The use of some cyclohexane-1,2-dicarboxylic acid esters as plasticizers is likewise known in the prior art. For example, the use of cyclohexanedicarboxylic acid dimethyl or diethyl esters (DE-A 28 23 165) and of cyclohexane-1,2-dicarboxylic acid di(2-ethylhexyl) ester (DE-A 12 63 296) as plasticizers in plastics has been described.

PCT/EP 98/08346 discloses that cyclohexanepolycarboxylic acids and derivatives thereof can be used as plasticizers. In this connection it is disclosed that, when compared with the phthalates mainly used hitherto as plasticizers, cyclohexanepolycarboxylic acids and derivatives thereof have lower density and viscosity and moreover, inter alia, also improve the low-temperature flexibility of the plastic over that achieved when using the corresponding phthalates as plasticizers. In addition, PCT/EP 98/08346 discloses that cyclohexanepolycarboxylic acids and derivatives thereof give better processing performance in the dry blend and in consequence an increased production rate, and also advantages in plastisol processing as a result of markedly lower viscosity compared with the corresponding phthalates. PCT/EP 98/08346 says nothing about

the toxicological properties of cyclohexanepolycarboxylic acids or of derivatives thereof.

It is an object of the present invention primarily to provide substances which can be used as plasticizers in plastics and which are suitable for this use both on the basis of their physical and material properties and moreover on the basis of their toxicological properties.

The production of liver tumors in rodents observed in relation to phthalates appears to be brought about by peroxisome proliferator-activated receptor-α (PPARα). The peroxisome proliferation underlying this mechanism can be detected using various indicators, inter alia, using the marked rise in absolute or relative liver weight, or else using the rise in certain enzyme activities, such as the specific activity of the cyanide-insensitive palmitoyl-CoA oxidase (Pal-CoA oxidase).

We have found that this object is achieved, surprisingly, in that cyclohexanepolycarboxylic acids and derivatives thereof, i.e. ring-hydrogenated benzenepolycarboxylic acids and derivatives thereof, unlike various conventional plasticizers, in particular phthalates and phthalate derivatives, do not bring about any biologically significant peroxisome proliferation and thus in relation to their physical and material properties and also from a toxicological point of view are more advantageous than these conventional plasticizers.

For the purposes of the present invention the cyclohexanepolycarboxylic acid or a derivative thereof or a mixture made from two or more thereof is regarded as toxicologically advantageous if when tested on rodents which have received a daily oral dose of 1000 mg/kg of body weight of this cyclohexanepolycarboxylic acid or of the derivative thereof or of the mixture made from two or more thereof via a stomach tube over a period of at least 14 days there is no statistically significant rise in the absolute liver weight or in the relative liver weight, i.e. in the liver weight based on the total body weight, and no toxicologically relevant rise in the specific enzyme activity of the cyanide-insensitive palmitoyl-CoA oxidase when comparison is made with the corresponding untreated control animals.

A statistically significant rise in the absolute or relative liver weight is usually present, for example in rats, if the rise in the absolute or relative liver weight of a test animal which has received a daily oral dose of 1000 mg of test substance/kg of

body weight via a stomach tube over a period of at least 14 days is more than 10% above the rise in the absolute or relative liver weight of a corresponding untreated control animal.

For the purposes of the present invention, a statistically significant rise in the absolute or relative liver weight is present in particular if the statistical rise in the absolute or relative liver weight of the test animal was determined by the Dunnett test (Dunnett, C.W. (1955), A multiple comparison procedure for comparing several treatments with a control, J. Am. Stat. Assoc. 50, 1096-1121; Dunnett, C.W. (1964), New tables for multiple comparisons with a control, Biometrics, 20, 482-491) to be more than 10% above that of the untreated control animal.

A toxicologically relevant rise in the specific activity of the cyanide-insensitive palmitoyl-CoA oxidase is present if the specific activity of the cyanide-insensitive palmityl-CoA oxidase measured in the liver homogenate of a test animal which has received a daily oral dose of 1000 mg of test substance/kg of body weight via a stomach tube over a period of at least 14 days is more than twice as high as the specific activity of the cyanide-insensitive palmitoyl-CoA oxidase determined in the liver homogenate of an untreated control animal.

The specific activity [mU/mg of protein] of the cyanide-insensitive palmitoyl-CoA oxidase is usually determined by the method of Lazarow (1981), Enzymology 72, 315-319, and the amount of protein in the liver homogenate is determined routinely by the protein-determination methods well known to the skilled worker, such as the Lowry method.

In addition, the cyclohexanepolycarboxylic acids and derivatives thereof which are toxicologically advantageous in the sense of the present invention are also likely to achieve relevant improvements in relation to reproduction-toxicology parameters when compared with conventional plasticizers, in particular with the phthalates and phthalic acid derivatives very frequently used for this purpose.

The present invention therefore provides the use of a cyclohexanepolycarboxylic acid or of a derivative thereof or of a mixture made from two or more thereof, which when tested on rodents at a daily oral dose of 1000 mg/kg of body weight via a stomach tube of the appropriate cyclohexanepolycarboxylic acid or of the derivative thereof or of the mixture made from two or more thereof over a period of at least 14 days causes no significant rise in the liver weight after the treatment

and does not cause a doubling of the specific activity of the cyanide-insensitive palmitoyl-CoA oxidase, measured in the liver homogenate, when comparison is made with untreated control animals, as a plasticizer for preparing toxicologically advantageous plastics.

For the purposes of the present invention, the term *"cyclohexanepolycarboxlic acids and derivatives thereof"* covers both the respective cyclohexanepolycarboxylic acids per se and derivatives thereof, in particular mono-, di- and, where appropriate, tri- and tetraesters, and also anhydrides of the cyclohexanepolycarboxylic acids. The esters used are alkyl, cycloalkyl or alkoxyalkyl esters, and the alkyl, cycloalkyl and alkoxyalkyl groups generally have from 1 to 30 carbon atoms, preferably from 2 to 20 carbon atoms and particularly preferably from 3 to 18 carbon atoms, and may be branched or linear.

Examples of specific compounds are:

Cyclohexane-1,4-dicarboxylic acid alkyl esters, e.g. cyclohexane-1,4-dicarboxylic acid monomethyl ester, cyclohexane-1,4-dicarboxylic acid dimethyl ester, cyclohexane-1,4-dicarboxylic acid diethyl ester, cyclohexane-1,4-dicarboxylic acid di-n-propyl ester, cyclohexane-1,4-dicarboxylic acid di-n-butyl ester, cyclohexane-1,4-dicarboxylic acid di-tert-butyl ester, cyclohexane-1,4-dicarboxylic acid diisobutyl ester, cyclohexane-1,4-dicarboxylic acid monoglycol ester, cyclohexane-1,4-dicarboxylic acid diglycol ester, cyclohexane-1,4-dicarboxylic acid di-n-octyl ester, cyclohexane-1,4-dicarboxylic acid diisooctyl ester, cyclohexane-1,4-dicarboxylic acid mono-2-ethylhexyl ester, cyclohexane-1,4-dicarboxylic acid di-2-ethylhexyl ester, cyclohexane-1,4-dicarboxylic acid di-n-nonyl ester, cyclohexane-1,4-dicarboxylic acid diisononyl ester, cyclohexane-1,4-dicarboxylic acid di-n-decyl ester, cyclohexane-1,4-dicarboxylic acid di-n-undecyl ester, cyclohexane-1,4-dicarboxylic acid diisodecyl ester, cyclohexane-1,4-dicarboxylic acid diisododecyl ester, cyclohexane-1,4-dicarboxylic acid di-n-octadecyl ester, cyclohexane-1,4-dicarboxylic acid diisooctadecyl ester, cyclohexane-1,4-dicarboxylic acid di-n-eicosyl ester, cyclohexane-1,4-dicarboxylic acid monocyclohexyl ester, cyclohexane-1,4-dicarboxylic acid dicyclohexyl ester;

Cyclohexane-1,2-dicarboxylic acid alkyl esters, e.g. cyclohexane-1,2-dicarboxylic acid monomethyl ester, cyclohexane-1,2-dicarboxylic acid dimethyl ester, cyclohexane-1,2-dicarboxylic acid diethyl ester, cyclohexane-1,2-dicarboxylic acid

di-n-propyl ester, cyclohexane-1,2-dicarboxylic acid di-n-butyl ester, cyclohexane-1,2-dicarboxylic acid di-tert-butyl ester, cyclohexane-1,2-dicarboxylic acid diisobutyl ester, cyclohexane-1,2-dicarboxylic acid monoglycol ester, cyclohexane-1,2-dicarboxylic acid diglycol ester, cyclohexane-1,2-dicarboxylic acid di-n-octyl ester, cyclohexane-1,2-dicarboxylic acid diisooctyl ester, cyclohexane-1,2-dicarboxylic acid di-2-ethylhexyl ester, cyclohexane-1,2-dicarboxylic acid di-n-nonyl ester, cyclohexane-1,2-dicarboxylic acid diisononyl ester, cyclohexane-1,2-dicarboxylic acid di-n-decyl ester, cyclohexane-1,2-dicarboxylic acid diisodecyl ester, cyclohexane-1,2-dicarboxylic acid di-n-undecyl ester, cyclohexane-1,2-dicarboxylic acid diisododecyl ester, cyclohexane-1,2-dicarboxylic acid di-n-octadecyl ester, cyclohexane-1,2-dicarboxylic acid diisooctadecyl ester, cyclohexane-1,2-dicarboxylic acid di-n-eicosyl ester, cyclohexane-1,2-dicarboxylic acid monocyclohexyl ester, cyclohexane-1,2-dicarboxylic acid dicyclohexyl ester;

Cyclohexane-1,3-dicarboxylic acid alkyl esters, e.g. cyclohexane-1,3-dicarboxylic acid monomethyl ester, cyclohexane-1,3-dicarboxylic acid dimethyl ester, cyclohexane-1,3-dicarboxylic acid diethyl ester, cyclohexane-1,3-dicarboxylic acid di-n-propyl ester, cyclohexane-1,3-dicarboxylic acid di-n-butyl ester, cyclohexane-1,3-dicarboxylic acid di-tert-butyl ester, cyclohexane-1,3-dicarboxylic acid diisobutyl ester, cyclohexane-1,3-dicarboxylic acid monoglycol ester, cyclohexane-1,3-dicarboxylic acid diglycol ester, cyclohexane-1,3-dicarboxylic acid di-n-octyl ester, cyclohexane-1,3-dicarboxylic acid diisooctyl ester, cyclohexane-1,3-dicarboxylic acid di-2-ethylhexyl ester, cyclohexane-1,3-dicarboxylic acid di-n-nonyl ester, cyclohexane-1,3-dicarboxylic acid diisononyl ester, cyclohexane-1,3-dicarboxylic acid di-n-decyl ester, cyclohexane-1,3-dicarboxylic acid diisodecyl ester, cyclohexane-1,3-dicarboxylic acid di-n-undecyl ester, cyclohexane-1,3-dicarboxylic acid diisododecyl ester, cyclohexane-1,3-dicarboxylic acid di-n-octadecyl ester, cyclohexane-1,3-dicarboxylic acid diisooctadecyl ester, cyclohexane-1,3-dicarboxylic acid di-n-eicosyl ester, cyclohexane-1,3-dicarboxylic acid monocyclohexyl ester, cyclohexane-1,3-dicarboxylic acid dicyclohexyl ester;

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n-butyl ester, cyclohexane-1,2,4-tricarboxylic acid di-tert-butyl ester, cyclohexane-1,2,4-tricarboxylic acid diisobutyl ester, cyclohexane-1,2,4-tricarboxylic acid monoglycol ester, cyclohexane-1,2,4-tricarboxylic acid diglycol ester, cyclohexane-1,2,4-tricarboxylic acid di-n-octyl ester, cyclohexane-1,2,4-tricarboxylic acid diisooctyl ester, cyclohexane-1,2,4-tricarboxylic acid di-2-ethylhexyl ester, cyclohexane-1,2,4-tricarboxylic acid di-n-nonyl ester, cyclohexane-1,2,4-tricarboxylic acid diisononyl ester, cyclohexane-1,2,4-tricarboxylic acid di-n-decyl ester, cyclohexane-1,2,4-tricarboxylic acid diisodecyl ester, cyclohexane-1,2,4-tricarboxylic acid di-n-undecyl ester, cyclohexane-1,2,4-tricarboxylic acid diisododecyl ester, cyclohexane-1,2,4-tricarboxylic acid di-n-octadecyl ester, cyclohexane-1,2,4-tricarboxylic acid diisooctadecyl ester, cyclohexane-1,2,4-tricarboxylic acid di-n-eicosyl ester, cyclohexane-1,2,4-tricarboxylic acid monocyclohexyl ester, cyclohexane-1,2,4-tricarboxylic acid dicyclohexyl ester and cyclohexane-1,2,4-tricarboxylic acid trimethyl ester, cyclohexane-1,2,4-tricarboxylic acid triethyl ester, cyclohexane-1,2,4-tricarboxylic acid tri-n-propyl ester, cyclohexane-1,2,4-tricarboxylic acid tri-n-butyl ester, cyclohexane-1,2,4-tricarboxylic acid tri-tert-butyl ester, cyclohexane-1,2,4-tricarboxylic acid triisobutyl ester, cyclohexane-1,2,4-tricarboxylic acid triglycol ester, cyclohexane-1,2,4-tricarboxylic acid tri-n-octyl ester, cyclohexane-1,2,4-tricarboxylic acid triisooctyl ester, cyclohexane-1,2,4-tricarboxylic acid tri-2-ethylhexyl ester, cyclohexane-1,2,4-tricarboxylic acid tri-n-nonyl ester, cyclohexane-1,2,4-tricarboxylic acid triisododecyl ester, cyclohexane-1,2,4-tricarboxylic acid tri-n-undecyl ester, cyclohexane-1,2,4-tricarboxylic acid triisododecyl ester, cyclohexane-1,2,4-tricarboxylic acid tri-n-octadecyl ester, cyclohexane-1,2,4-tricarboxylic acid triisooctadecyl ester, cyclohexane-1,2,4-tricarboxylic acid tri-n-eicosyl ester, cyclohexane-1,2,4-tricarboxylic acid tricyclohexyl ester;

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octadecyl ester, cyclohexane-1,2,3-tricarboxylic acid diisooctadecyl ester, cyclohexane-1,2,3-tricarboxylic acid di-n-eicosyl ester, cyclohexane-1,2,3-tricarboxylic acid monocyclohexyl ester, cyclohexane-1,2,3-tricarboxylic acid dicyclohexyl ester and cyclohexane-1,2,3-tricarboxylic acid trimethyl ester, cyclohexane-1,2,3-tricarboxylic acid triethyl ester, cyclohexane-1,2,3-tricarboxylic acid tri-n-propyl ester, cyclohexane-1,2,3-tricarboxylic acid tri-n-butyl ester, cyclohexane-1,2,3-tricarboxylic acid tri-tert-butyl ester, cyclohexane-1,2,3-tricarboxylic acid triisobutyl ester, cyclohexane-1,2,3-tricarboxylic acid triglycol ester, cyclohexane-1,2,3-tricarboxylic acid tri-n-octyl ester, cyclohexane-1,2,3-tricarboxylic acid triisooctyl ester, cyclohexane-1,2,3-tricarboxylic acid tri-2-ethylhexyl ester, cyclohexane-1,2,3-tricarboxylic acid tri-n-nonyl ester, cyclohexane-1,2,3-tricarboxylic acid triisododecyl ester, cyclohexane-1,2,3-tricarboxylic acid tri-n-undecyl ester, cyclohexane-1,2,3-tricarboxylic acid triisododecyl ester, cyclohexane-1,2,3-tricarboxylic acid tri-n-octadecyl ester, cyclohexane-1,2,3-tricarboxylic acid triisooctadecyl ester, cyclohexane-1,2,3-tricarboxylic acid tri-n-eicosyl ester, cyclohexane-1,2,3-tricarboxylic acid tricyclohexyl ester;

Cyclohexane-1,2,4,5-tetracarboxylic acid alkyl esters, e.g. cyclohexane-1,2,4,5-tetracarboxylic acid monomethyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid dimethyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid diethyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid di-n-propyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid di-n-butyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid di-tert-butyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid diisobutyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid monoglycol ester, cyclohexane-1,2,4,5-tetracarboxylic acid diglycol ester, cyclohexane-1,2,4,5-tetracarboxylic acid di-n-octyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid diisooctyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid di-2-ethylhexyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid di-n-nonyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid diisononyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid di-n-decyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid diisodecyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid di-n-undecyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid diisododecyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid di-n-octadecyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid diisooctadecyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid di-n-eicosyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid monocyclohexyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid trimethyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid triethyl ester, cyclohexane-1,2,4,5-

tetracarboxylic acid tri-n-propyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tri-n-butyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tri-tert-butyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid triisobutyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid triglycol ester, cyclohexane-1,2,4,5-tetracarboxylic acid tri-n-octyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid triisooctyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tri-2-ethylhexyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tri-n-nonyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid triisododecyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tri-n-undecyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid triisododecyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tri-n-octadecyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid triisooctadecyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tri-n-eicosyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tricyclohexyl ester and cyclohexane-1,2,4,5-tetracarboxylic acid tetramethyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tetraethyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tetra-n-propyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tetra-n-butyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tetra-tert-butyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tetraisobutyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tetraglycol ester, cyclohexane-1,2,4,5-tetracarboxylic acid tetra-n-octyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tetraisooctyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tetra-2-ethylhexyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tetra-n-nonyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tetraisododecyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tetra-n-undecyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tetraisododecyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tetra-n-octadecyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tetraisooctadecyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tetra-n-eicosyl ester, cyclohexane-1,2,4,5-tetracarboxylic acid tetracyclohexyl ester;

anhydrides of cyclohexane-1,2-dicarboxylic acid, cyclohexane-1,2,4-tricarboxylic acid, cyclohexane-1,2,3-tricarboxylic acid and cyclohexane-1,2,4,5-tetracarboxylic acid.

The cyclohexane-1,2-dicarboxylic acid esters disclosed in PCT/EP 98/08346 and listed again below are also toxicologically advantageous in the sense of the present invention:

Cyclohexane-1,2-dicarboxylic acid di(isopentyl) ester obtainable by hydrogenating di(isopentyl) phthalate with Chemical Abstracts Registry Number (hereinafter: CAS No.) 84777-06-0;

cyclohexane-1,2-dicarboxylic acid di(isoheptyl) ester obtainable by hydrogenating di(isoheptyl) phthalate with CAS No. 71888-89-6;

cyclohexane-1,2-dicarboxylic acid di(isononyl) ester obtainable by hydrogenating a di(isononyl) phthalate with CAS No. 68515-48-0;

cyclohexane-1,2-dicarboxylic acid di(isononyl) ester obtainable by hydrogenating a di(isononyl) phthalate with CAS No. 28553-12-0, based on n-butene;

cyclohexane-1,2-dicarboxylic acid di(isononyl) ester obtainable by hydrogenating a di(isononyl) phthalate with CAS No. 28553-12-0, based on isobutene;

a 1,2-di-C_9 ester of cyclohexanedicarboxylic acid obtainable by hydrogenating a di(nonyl) phthalate with CAS No. 68515-46-8;

a cyclohexane-1,2-dicarboxylic acid di(isodecyl) ester obtainable by hydrogenating a di(isodecyl) phthalate with CAS No. 68515-49-1;

A 1,2-di-C_{7-11} ester of cyclohexanedicarboxylic acid obtainable by hydrogenating the corresponding phthalic ester with CAS No. 68515-42-4;

1,2-di-C_{7-11} esters of cyclohexanedicarboxylic acid obtainable by hydrogenating the di-C_{7-11} phthalates with the following CAS Nos:

111 381-89-6,
111 381 90-9,
111 381 91-0,
68515-44-6,
68515-45-7 and
3648-20-7;

a 1,2-di-C_{9-11} ester of cyclohexanedicarboxylic acid obtainable by hydrogenating a di-C_{9-11} phthalate with CAS No. 98515-43-5;

a 1,2-di(isodecyl) ester of cyclohexanedicarboxylic acid obtainable by hydrogenating a di(isodecyl) phthalate composed mainly of di(2-propylheptyl) phthalate;

a 1,2-di-C_{7-9} ester of cyclohexanedicarboxylic acid obtainable by hydrogenating the corresponding phthalic ester which has branched-chain or linear C_{7-9}-alkyl ester groups; examples of corresponding phthalates which may be used as starting materials have the following CAS Nos:

di-C_{7-9}-alkyl phthalate with CAS No. 111 381-89-6;
di-C_7-alkyl phthalate with CAS No. 68515-44-6; and
di-C_9-alkyl phthalate with CAS No. 68515-45-7.

The entire content of PCT/EP 98/08346, which relates, inter alia, to those compounds just listed and to the preparation of benzenepolycarboxylic acids using specific macroporous catalysts, is incorporated into the present application by way of reference.

Other products which are toxicologically advantageous in the sense of the present invention are the hydrogenation products of the commercially available benzenecarboxylic acid esters with the trade names Jayflex DINP (CAS No. 68515-48-0), Jayflex DIDP (CAS No. 68515-49-1), Palatinol 9-P, Vestinol 9 (CAS No. 28553-12-0), TOTM-I (CAS No. 3319-31-1), Linplast 68-TM and Palatinol N (CAS No. 28553-12-0).

The cyclohexanepolycarboxylic acids and derivatives thereof which are toxicologically advantageous in the sense of the present invention may be used in any of the plastics known to the skilled worker, in particular in bulk plastics, such as PVC, PVB and PVAc.

An example will now be used to explain the invention in greater detail.

EXAMPLE

The results listed in Table 1 were obtained after oral administration of 1000 mg/kg of body weight of the test substance cyclohexane-1,2-dicarboxylic acid diisononyl ester via a stomach tube over a period of 14 days to female Wistar rats.

Parameter	Group 0 (Control group; n = 10) [Average ± standard deviation]	Group 1 (n = 10) (Test group: 1000 mg of test substance/kg of body weight daily by stomach tube) [Average ± standard deviation]
Body weight [g]	400.3 ± 29.7	398.9 ± 28.5
Absolute liver weight [g]	19.21 ± 2.64	19.64 ± 1.77
Relative liver weight based on body weight [%]	4.79 ± 0.37	4.93 ± 0.41
Palmitoyl-CoA oxidase	6.20 ± 0.38	7.24 ± 0.87*

[mU/mg of protein]		

*Statistically significant change by the Mann-Whitney U test (cf., for example, Hollander, M. and Wolfe, D.A. (1973), Nonparametric Statistical Methods, John Wiley and Sons Inc., N.Y.), but toxicologically irrelevant.

Table 1: Results from determination of absolute and relative rise in liver weight and from determination of palmitoyl-CoA oxidase activity in female Wistar rats in (a) the control group (10 untreated animals) and (b) the test group (10 animals which have received a daily oral dose of 1000 mg/kg of body weight of the test substance cyclohexane-1,2-dicarboxylic acid diisononyl ester via a stomach tube over a period of at least 14 days).

Statistical evaluation for determination of absolute and relative liver weight used the Dunnett test, and specific activity of the cyanide-insensitive palmitoyl-CoA oxidase was determined using the method of Lazarow (1981), Enzymology 72, 315-319.

We claim:

1. The use of a cyclohexanepolycarboxylic acid or of a derivative thereof or of a mixture made from two or more thereof, which when tested on rodents at a daily oral dose of 1000 mg/kg of body weight via a stomach tube of the appropriate cyclohexanepolycarboxylic acid or of the derivative thereof or of the mixture made from two or more thereof over a period of at least 14 days causes no significant rise in the liver weight after the treatment and does not cause a doubling of the specific activity of the cyanide-insensitive palmitoyl-CoA oxidase, measured in the liver homogenate, compared with untreated control animals, as a plasticizer for preparing toxicologically advantageous plastics.

2. The use as claimed in claim 1, wherein the cyclohexanepolycarboxylic acid or the derivative thereof or the mixture made from two or more thereof is selected from the group consisting of ring-hydrogenated mono- and dialkyl esters of phthalic acid, isophthalic acid or terephthalic acid, ring-hydrogenated mono-, di- and trialkyl esters of trimellitic acid, of trimesic acid or of hemimellitic acid, mono-, di-, tri- and tetraalkyl esters of pyromellitic acid, where the alkyl groups may be linear or branched and in each case have from 1 to 30 carbon atoms, ring-hydrogenated anhydrides of phthalic acid, trimellitic acid, trimesic acid or hemimellitic acid, pyromellitic dianhydride and mixtures made from two or more of these.

3. The use as claimed in claim 1, wherein the cyclohexanepolycarboxylic acid or the derivative thereof or the mixture made from two or more thereof is selected from the group consisting of:

cyclohexane-1,2-dicarboxylic acid di(isopentyl) ester obtainable by hydrogenating di(isopentyl) phthalate with Chemical Abstracts Registry Number (hereinafter: CAS No.) 84777-06-0;

cyclohexane-1,2-dicarboxylic acid di(isoheptyl) ester obtainable by hydrogenating di(isoheptyl) phthalate with CAS No. 71888-89-6;

cyclohexane-1,2-dicarboxylic acid di(isononyl) ester obtainable by hydrogenating a di(isononyl) phthalate with CAS No. 68515-48-0;

cyclohexane-1,2-dicarboxylic acid di(isononyl) ester obtainable by hydrogenating a di(isononyl) phthalate with CAS No. 28553-12-0, based on n-butene;

cyclohexane-1,2-dicarboxylic acid di(isononyl) ester obtainable by hydrogenating a di(isononyl) phthalate with CAS No. 28553-12-0, based on isobutene;

a 1,2-di-C_9 ester of cyclohexanedicarboxylic acid obtainable by hydrogenating a di(nonyl) phthalate with CAS No. 68515-46-8;

a cyclohexane-1,2-dicarboxylic acid di(isodecyl) ester obtainable by hydrogenating a di(isodecyl) phthalate with CAS No. 68515-49-1;

a 1,2-di-C_{7-11} ester of cyclohexanedicarboxylic acid obtainable by hydrogenating the corresponding phthalic ester with CAS No. 68515-42-4;

a 1,2-di-C_{7-11} ester of cyclohexanedicarboxylic acid obtainable by hydrogenating the di-C_{7-11} phthalates with the following CAS Nos:
111 381-89-6,
111 381 90-9,
111 381 91-0,
68515-44-6,
68515-45-7 and
3648-20-7;

a 1,2-di-C_{9-11} ester of cyclohexanedicarboxylic acid obtainable by hydrogenating a di-C_{9-11} phthalate with CAS No. 98515-43-5;

a 1,2-di(isodecyl) ester of cyclohexanedicarboxylic acid, obtainable by hydrogenating a di(isodecyl) phthalate composed mainly of di(2-propylheptyl) phthalate;

a 1,2-di-C_{7-9} ester of cyclohexanedicarboxylic acid, obtainable by hydrogenating the corresponding phthalic ester which has branched-chain or linear C_{7-9}-alkyl ester groups.